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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,408	12/07/2001	John J. Castellot JR.	MBI-004CN	6101
959	7590	05/28/2004	EXAMINER	
LAHIVE & COCKFIELD, LLP. 28 STATE STREET BOSTON, MA 02109			MARTINELL, JAMES	
			ART UNIT	PAPER NUMBER
			1631	
DATE MAILED: 05/28/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/010,408	Applicant(s) CASTELLOT, JOHN J.	
	Examiner James Martinell	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 22 March 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-10, 13, 16-21, 48, 58 and 60 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10, 13, 16-21, 48, 58 and 60 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 April 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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Claim 58 is drawn to two independent and distinct methods (parts (i) and (ii) are drawn to assays of nucleic acids and part (iii) is drawn to a protein assay method) and thus ought to have been placed in both Groups I and IX in the requirement for restriction mailed May 2, 2003. The error is regretted. Claim 58 is now grouped in both Groups I and IX. Since applicants have already elected Group I, part (iii) of claim 58 is withdrawn as being drawn to a nonelected invention. Applicants may traverse this restriction in their next response.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 7, 10, 17-21, 48, 58, and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are vague, indefinite, and incomplete.

- (a) The recitation of "HICP" (claims 10, 20, 21, 48, 58, and 60) is vague and indefinite. This rejection is repeated for reasons already of record (*e.g.*, Office action mailed September 22, 2003, page 2, item (b)). Applicants' arguments (response filed March 22, 2004, pages 6-7) are not persuasive because the definition on page 1, lines 32-34 of the specification is vague and indefinite. The definition referred to by applicants reads, "The present invention provides a novel nucleic acid molecule which encodes a protein, referred to herein as Heparin-Induced, CCN-like protein (HICP), which is capable of modulating a variety of cellular processes including cell proliferation." The inclusion of "a variety of cellular processes" in the definition renders the metes and bounds of the claims unclear. It is noted that the instant claims do not recite activities for the protein, as do claims 1 and 7.
- (b) The recitation of "capable of specifically hybridizing to" (claim 7) is vague and indefinite. This rejection is repeated for reasons already of record (*e.g.*, Office action mailed September 22, 2003, page 2, item (c)). Applicants' arguments

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(response filed March 22, 2004, page7) are not persuasive because applicants do not address the issue of the presence of other molecules in the reaction mixture. The term "specifically hybridizing" is a relative one with no frame of reference given, rendering the claim incomplete.

- (c) Claim 58 is vague and indefinite because it claims more than was elected (see the supplemental requirement for restriction above.

Claims 1, 7, 8, and 16-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for those sequences recited with specificity, does not reasonably provide enablement for sequences that have 90% homology to certain SEQ ID NOs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is repeated for reasons already of record (*e.g.*, Office action mailed September 22, 2003, page 4). Applicants' arguments (response filed March 22, 2004, pages 12-13) are not convincing. The CAFC in *In re Wands* (*In re Wands*, 8 USPQ2d 1400, Fed Cir. 1988) listed various factors to be considered in determining enablement. They include:

- (1) The quantity of experimentation necessary
- (2) The amount of direction or guidance presented
- (3) The presence or absence of working examples
- (4) The nature of the invention
- (5) The state of the prior art
- (6) The relative skill of those in the art
- (7) The predictability of the art
- (8)

Each of these factors is discussed below.

*The quantity of experimentation necessary*

The quantity of experimentation necessary to find other active embodiments of the sequences embraced by the claims is high because the assays (*e.g.*, pages 7, 18, 52-54, 58, and 61-62) disclosed in the instant application are all time-consuming and cumbersome assays that require either whole organisms for bioassays, cells in culture and complex molecular assays following exposure to a putative active HICP mutant protein. The putative HICP mutant protein must first be synthesized in a complex series of molecular manipulations that involve mutation of a nucleic acid sequence, molecular cloning of the mutated sequence, and expression in host cells (*e.g.*, 60-61).

*The amount of direction or guidance presented*

The instant application provides no direction or guidance as to which parts or residues of the HICP molecule may be altered while still retaining at least one HICP activity.

*The presence or absence of working examples*

There are no working examples of a modified HICP protein. The application contains examples drawn only to naturally occurring HICP.

*The nature of the invention*

The invention is in the fields of molecular biology, recombinant DNA, and protein purification.

*The state of the prior art*

There is no prior art of record in connection with the creation of mutant forms of HICP.

*The relative skill of those in the art*

The relative skill of those in the art is high. The person with skill in the art most likely in possession of a Ph.D. degree and at least some post-doctoral research experience.

*The predictability of the art*

The art of prediction of three-dimensional structure (and thus activity) of proteins is in its infancy. Bourne (in *Structural Bioinformatics*, 2003, Bourne et al (eds.), Wiley-Liss, Inc., pp. 499-505). in the section bridging pages 502-503 discloses that three-dimensional structural prediction of polypeptides for which little is known experimentally in connection with 3-D structure is low (*e.g.*, see the paragraph bridging pages 502-503). The instant application teaches nothing in regard to the 3-D structure of HICP.

*The breadth of the claims*

The claims are very broad in that they embrace (at least as the number of sequences to be tested) no fewer than  $8.0 \times 10^{244}$  embodiments of sequences that are at least 90% homologous to SEQ ID NO: 1, no fewer than  $5.5 \times 10^{66}$  embodiments that are at least 90% homologous to SEQ ID NO: 2, and  $7.3 \times 10^{149}$  embodiments that are at least 90% homologous to SEQ ID NO: 3.

After consideration of all of these factors, the claims are deemed not enabled for their full scope.

Claims 1-10, 13, 16-21, 48, 58, and 60 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. This rejection is repeated for reasons already of record (*e.g.*, Office action mailed September 22, 2003, pages 4-5). Applicants' arguments (response filed March 22, 2004, pages 13-14) are not convincing. The disclosure of the activities of HICP is not an indication of usefulness within the meaning of 35 USC § 101 because it is not evident that any of those activities obtains *in vivo*. Thus, the invention lacks specific, substantial, and credible utility in its current form (see *Brenner v. Manson*, Supreme Court of the U.S., 148 USPQ 689 (1966)).

Claims 1-10, 13, 16-21, 48, 58, and 60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

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described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The discussion in the rejection under 35 USC § 101 is incorporated here.

Claims 1, 7, and 10 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Bonaldo et al (Genome Res. 6: 791 (1996)). This rejection is repeated for reasons already of record (*e.g.*, Office action mailed September 22, 2003, page 5). Applicants' arguments (response filed March 22, 2004, pages 15-16) are not convincing because the DNA of Bonaldo et al has all of the structural elements of the claims. A global alignment of the sequences is not appropriate here because the claims are open. In addition, the DNA of Bonaldo et al would hybridize under stringent conditions to SEQ ID NO: 1 (*e.g.*, see claims 1 and 7).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James Martinell whose telephone number is (571) 272-0719. The fax phone number for Examiner Martinell's desktop workstation is (571) 273-0719. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be e-mailed to [james.martinell@uspto.gov](mailto:james.martinell@uspto.gov). Since e-mail communications may not be secure, it is suggested that information in such requests be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

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**PLEASE NOTE THE NEW FAX NUMBER**

The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.



**James Martinell, Ph.D.**  
**Primary Examiner**  
**Art Unit 1631**

5/27/04